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10/014,731	12/11/2001	Joseph A. Monforte	24743-2308	5775

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FISH & RICHARDSON, PC
12390 EL CAMINO REAL
SAN DIEGO, CA 92130-2081

EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,731	MONFORTE, JOSEPH A.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *29-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/10/02,02/25/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-28 in the reply filed on May 27, 2004 is acknowledged.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an assay in which polypeptide binding components are attached to a solid substrate are contacted with sample and genetic packages that comprise a polypeptide binding component and a predetermined marker component, does not reasonably provide enablement for a method wherein only the genetic package is contacted with the sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

4. Claim 1 is rejected under 35 U.S.C. 112, first paragraph a step of contacting a polypeptide binding component which is attached to a solid substrate with the sample and the genetic packages is critical or essential to the practice of the invention, but not included in the claim(s). Also a wash step to remove unbound genetic packages is essential, because if the unbound genetic packages are not removed, the marker

component will always be detected regardless if binding has occurred or not and thus false positive results will occur.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear what relationship exits between the polypeptide-binding component and the marker component. The genetic package comprises the polypeptide-binding component and the marker component which are independent from one another and thus it is unclear how the one or more polypeptides is detected using these two components. For example, regardless if the polypeptide-binding component binds one or more polypeptides, the marker component will be detected. Thus, even when no binding occurs to the one or more polypeptides the marker component will be detected and a false positive result will occur. Please clarify.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step of contacting a polypeptide binding component which is attached to a solid substrate with the sample and the genetic packages and also a wash step to remove unbound material, and a release step for releasing the polypeptide before the amplifying step.

Claim 1 is vague and indefinite because it is unclear how more than one polypeptide can be detected. The claim in lines 7 & 8 recites "the polypeptide binding component specifically binds to at least one of the polypeptides", if the polypeptide specifically bind to one polypeptide, how can say twenty polypeptides be detected by the polypeptide binding component that specifically binds to one polypeptide? Please clarify.

Claim 12 is vague and indefinite because of the use of a symbol: ie λ. Although the symbol may have art-recognized meanings, it is unclear if applicant intends to claim the prior art symbols. The symbol should be defined in its first instance.

Claim 13, line 2 "plurality of bio-displayed polypeptide binding components" is vague and indefinite because it is unclear if applicant is applying many of the same kind of the bio-displayed polypeptide binding components or if applicant is applying many different kinds of bio-displayed polypeptide binding components.

Claim 13 is vague and indefinite because it is unclear what relationship exits between the genetic package and the bio-displayed polypeptide binding components. Does the genetic package comprise the bio-displayed polypeptide which binds to the target polypeptide or are the genetic package and the bio-display polypeptides considered independent of one another? Does a single genetic package comprise a plurality of bio-displayed polypeptide binding components? Further, it is unclear what relationship exits between the bio-displayed polypeptide binding components and the polypeptide-binding components recited in claim 1. Are the bio-displayed polypeptide binding components suppose to replace the polypeptide binding components in claim

1? What relationship exits between the genetic package, the polypeptide binding components and the bio-displayed polypeptide binding components? Please clarify.

Claim 16, line 2 "associated with" is vague and indefinite. It is unclear how the bio-displayed polypeptide binding components is associated with a different marker component. Does each and every bio-displayed polypeptide binding component comprise a different marker protein or are they related in some other manner?

Claim 17, line 2 "related marker components" is vague and indefinite. It is unclear how the marker components are related. More particularly, claim 16 recites that the marker components are different and then claim 17 recites related. Please clarify.

Claim 24, line 2 the recitation "signature polypeptide" is vague and indefinite. It is unclear what applicant is referring to. There is no definition provided for the term in the specification. Please clarify.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-5, 10-12, 18 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Li (WO 97/44491) in light of Ward et al (US 5,741,668)

Li discloses methods of detection using bacteriophages (genetic package). Li disclose that polypeptides can be detected using these bacteriophages (abstract & page 6). Li disclose that these bacteriophages (genetic package) comprise ligands

(polypeptide-binding component) that specifically bind to a selected polypeptide (p. 8, lines 1-5). Li disclose that the bacteriophage (genetic package) can comprise a label such as green fluorescent protein (marker component) (p. 10, lines 1-20). Li disclose that the bacteriophage can be M13 (p. 7, lines 1-3). Li discloses amplifying the phage (p. 20). Li disclose that the polypeptide can be immobilized to a solid substrate such as a nitrocellulose filter or elisa (p. 14, lines 1-31). Li disclose that the sample can be a blood sample (p. 6, lines 8-15). Li disclose a wash steps (p. 20-21) to remove unbound material.

With respect to the amplifying step as recited in the instant claims, the claims utilize comprising language and therefore the amplifying step could be performed before step (a) and therefore, Li teaches amplifying as recited in the instant claims.

With respect to the predetermined marker component as recited in the instant claims, the applicant defines predetermined marker component on page 12 of the specification as a peptide, a nucleotide, a polypeptide, or the like. Since Li teaches a label, which can be a green fluorescent protein, which is known in the art to be a polypeptide (Ward et al., teaches that GFP is a polypeptide), Li teaches a marker component as instantly recited.

9. Claims 1-4, 18-20 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Sano et al (Us 5,665,539).

Sano et al disclose methods of detecting antigens such as proteins (col 2, lines 32-39). Sano et al disclose a complex comprising nucleic acid markers conjugated to antibodies (col 10, lines 24-28). Sano et al disclose that these nucleic acid markers are

conjugated to the antibodies by a linker molecule (col 4, lines 24-65). Sano et al disclose that these antibodies bind to the antigen to be detected. Therefore, Sano teaches a complex (genetic package) comprising antibodies (polypeptide binding component) and a nucleic acid marker (marker component). Sano et al disclose amplifying the marker by PCR (col 6, line 34 – col 7). Sano et al disclose the analyte bound to a solid support (col 3, lines 49-53 & col 10, lines 1-5). Sano et al disclose that by using many different DNA markers attached to different antibodies and by using specific PCR primers for each DNA marker at the PCR amplification stem, many different antigens can be simultaneously detected (col 10, lines 20-24).

With respect to detecting polypeptides as recited in the instant claims. Sano et al teaches detecting proteins and according to applicant's definition on page 10, lines 13-16 of the specification "the terms "polypeptide," "peptide," and "protein" are used interchangeably to refer to a polymer of amino acids linked through peptide bonds. Polypeptides of the include, but are not limited to, proteins". Therefore, Sano et al teaches the detection of polypeptides.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 6-9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li.

See above for teachings of Li.

Li fail to specifically teach detecting at the amounts of polypeptides as instantly recited.

Li teaches that the bacteriophages express on its surface at least 10, or at least 100, or at least 400, or at least 800, or at least 1000 copies of the ligand which bind to the polypeptides to be detected (p. 9). Although Li does not specifically teach the number of polypeptides detected, Li does teach the number of ligands used to bind the polypeptides.

With respect to the numbers of polypeptides to be detected as recited in the instant claims. The optimal number of ligands to detect the polypeptides can be determined by routine experimentation and thus it would have been obvious to one of ordinary skill in the art to optimize the number of ligands to correspond with the number of polypeptides. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions

of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

With respect to claim 13 as recited in the instant claims because it is unclear what relationship exits between the polypeptide-binding component, genetic package and bio-displayed polypeptide binding component and it is also unclear what relationship exits between the bio-displayed polypeptide binding components and the polypeptide-binding components recited in claim 1. Are the bio-displayed polypeptide binding components suppose to replace the polypeptide binding components in claim 1 (see 112 rejections above concerning claim 13) and further, it would have been obvious to one or ordinary skill in the art that the bacteriophages of Li would have a plurality of polypeptide-binding components. Therefore, Li et al teaches a plurality of bio-displayed polypeptides as recited in the instant claims.

13. Claims 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sano et al.

See above for teachings of Sano et al.

Sano et al differ from the instant invention in failing to teach the amount of different polypeptide binding components.

With respect to claim 13 as recited in the instant claims because it is unclear what relationship exits between the polypeptide-binding component, genetic package

and bio-displayed polypeptide binding component and it is also unclear what relationship exits between the bio-displayed polypeptide binding components and the polypeptide-binding components recited in claim 1. Are the bio-displayed polypeptide binding components suppose to replace the polypeptide binding components in claim 1 (see 112 rejections above concerning claim 13) and further, it would have been obvious to one or ordinary skill in the art that the genetic package of Sano would have a plurality of polypeptide-binding components and since Sano teaches different antibody complexes for different antigens, Sano therefore teaches a plurality of bio-displayed antibodies as recited in the instant claims.

With respect to the amount of different polypeptide-binding components as recited in the instant claims. The optimal amount of different polypeptide-binding components can be determined by routine experimentation and thus it would have been obvious to one of ordinary skill in the art to optimize the amount of polypeptide-binding components. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

14. Claims 22, 23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li in view of Buechler et al (US 5,939,272).

See above for teachings of Li.

Li differs from the instant invention in failing to teach determining an amount of the marker component.

Buechler et al disclose ligand-receptor assays such as sandwich assays which are used for the quantification of an analyte. Buechler et al disclose using receptors in excess over the concentrtion of ligand to be determined in an assay (col 2, lines 1-8). Buechler et al disclose that these assays are useful for the in vitro determination of the presence and concentration of ligands in fluids (col 1, lines 32-67).

It would have been obvious to use receptors in excess as taught by Buechler et al in the method of Li because Li teaches that assays such as sandwich assays can be used to determine binding between a protein, such as a receptor and a ligand and Buechler et al teaches that using receptors in excess over the concentration of ligand provides for the in vitro determination of the presence and concentration of ligands in fluids.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Teodorescu et al (US 4,797,363) et al disclose bacteriophages employed as agents for recognition and identification of molecules and cellular materials.

Ladner et al (US 5,837,500) disclose genetic package comprising a binding domain displayed on its surface (abstract).

Nock et al (US 6,686,154) et al disclose bacteriophages having polypeptides on their surface. Nock et al discloses amplifying the phage.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
July 20, 2004

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
07/23/04